



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/588,929	08/09/2006	Christopher P. Regan	21396P	4283
210 MERCK P O BOX 2000 RAHWAY, NJ 07065-0907	7590 12/07/2010		<div>EXAMINER</div> <div>SCHLIENTZ, LEAH H</div>	
			<div>ART UNIT</div> <div>1618</div>	<div>PAPER NUMBER</div>
			<div>MAIL DATE</div> <div>12/07/2010</div>	<div>DELIVERY MODE</div> <div>PAPER</div>

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/588,929

Applicant(s)

REGAN, CHRISTOPHER P.

Examiner

Leah Schlientz

Art Unit

1618

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 01 October 2010.
2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1 and 5-9 is/are pending in the application.
4a) Of the above claim(s) 5-8 is/are withdrawn from consideration.
5) ☐ Claim(s) _____ is/are allowed.
6) ☒ Claim(s) 1 and 9 is/are rejected.
7) ☐ Claim(s) _____ is/are objected to.
8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/22)
4) ☐ Interview Summary (PTO-413)
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____
Paper No(s)/Mail Date _____

DETAILED ACTION

Acknowledgement of Receipt

Applicant's Response, filed 10/1/2010, in reply to the Office Action mailed 7/2/2010, is acknowledged and has been entered. Claims 1 and 9 have been amended. Claims 1 and 5-9 are pending, of which claims 5-8 are withdrawn from consideration at this time as being drawn to a non-elected invention. Claims 1 and 9 are readable upon the elected invention and are examined herein on the merits for patentability.

Response to Arguments

Any rejection not reiterated herein has been withdrawn.

Applicant's arguments, with regard to the rejection of claims 1 and 9 under 35 U.S.C. 102(b) as being anticipated by Donahue *et al.* (US 2005/0155101), have been fully considered. The rejection is withdrawn with regard to claim 1, as being overcome by amendment. The rejection is maintained with regard to claim 9, for reasons set forth hereinbelow.

Applicant's arguments, with regard to the rejection of claims 1 and 9 under 35 U.S.C. 103(a) as being unpatentable over Pugsley *et al.* (*J. Cardiovascular Pharmacology*, 1998, 32(6), p. 863-874) and Gehrmann *et al.* (*J. Cardiovascular Electrophysiology*, 2000, 11(3), p. 354-368), in view of Knobloch (*Naunyn-*

Schmiedeberg's Arch Pharmacol., 2002, 366, p. 482-487), have been fully considered, but are moot in view of new grounds of rejection set forth hereinbelow.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 9 is rejected under 35 U.S.C. 102(b) as being anticipated by Donahue *et al.* (US 2002/0155101).

Donahue discloses methods of treating or preventing cardiac arrhythmia including administering an amount of at least one polynucleotide that modulates an electrical property of the heart (abstract). Preferred mammals include rats (paragraphs 0035-0036). Methods include administration routes that directly or indirectly result in increase in AV node refractory period (AVNERP) as measured by the assay. Conventional methods for detecting and measuring AVNERP are known and include standard electrophysiological tests. The polynucleotide is further introduced into cardiac tissue and expressing the same sufficient to detectably increase heart rate as determined by standard electrocardiogram (ECG) recording. A preferred polynucleotide: 1) either decreases the A-H interval or increases the AVNERP by at least about 10% as determined by electrophysiology assay; and 2) decreases ventricular response rate or pulse rate during a trial fibrillation by at least 10% as

determined by a standard electrocardiogram (ECG) reading (paragraphs 0040-043). Additionally preferred polynucleotides include those encoding at least one ion channel protein, including K channel (paragraph 0044). Specific reference to "standard electrophysiology assay" includes 1) providing a mammalian heart (in vivo or ex vivo), 2) contacting the heart with at least one suitable polynucleotide, 3) transferring the polynucleotide into cells of the heart under conditions which allow expression of the encoded amino acid sequence, and 4) detecting modulation (increase or decrease) of at least one electrical property in the transformed heart (at least one of conduction, ventricular response rate and pulse rate) (paragraphs 0082-0087). Illustrative strategies for detecting modulation of transformed heart include ECG. More specific methods preventing or treating cardiac arrhythmia include overexpressing a k channel protein subunit sufficient to decrease surface ECG repolarization by at least 5% (paragraphs 0091-0092). See also Examples 1-2, including measurement of QRS, QT, A-H, H-V intervals and AVNERP.

Response to Arguments

Applicant argues on page 4 of the Response that claim 9 has been amended to incorporate the limitations of dependent claims 10 and 11. Entry of the amendments is respectfully requested. Claims 1, 9 and 10 were rejected under 35 USC 102(b) as anticipated by Donahue, et al. Donahue, et al., describe gene therapy methods for treating and preventing cardiac arrhythmia. With the amendments of claim 9 described above, Applicants respectfully maintain that the claims are not anticipated by Donahue, et al.

This is not found to be persuasive. It is noted that previously pending claim 11 was not rejected by the Donahue reference. However, the limitation from previous claim 11 which has been introduced into claim 9 (i.e. that a compound effects the potassium ion channel, the sodium ion channel, and the calcium ion channel *secondarily through binding to a muscarinic, adenosinergic receptor or serotoninergic receptor*) is listed in the alternative. Therefore, it is considered that the Donahue reference meets the limitations of claim 9 as previously applied, and the rejection is maintained.

New Grounds for Rejection

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pugsley *et al.* (*J. Cardiovascular Pharmacology*, 1998, 32(6), p. 863-874) and Gehrmann *et al.* (*J. Cardiovascular Electrophysiology*, 2000, 11(3), p. 354-368), in view of Knobloch (*Naunyn-Schmiedeberg's Arch Pharmacol.*, 2002, 366, p. 482-487), in further view of Rotolo (US 5,445,149).

Pugsley discloses sodium channel-blocking properties of spiradoline, a kappa receptor agonist and its antiarrhythmic action in the rat (page 1). Male Sprague-Dawley rats were used for whole animal studies. Intact rats were anesthetized with pentobarbital and the trachea cannulated for artificial ventilation. The right jugular vein and left carotid artery were cannulated for administration of drugs and recording of blood pressure, respectively. ECG was recorded. By using intact rats described, electrical stimulation of the left ventricle was accomplished via two Teflon-coated silver wire stimulating electrodes inserted through the chest wall and implanted into the left ventricle. Ventricular fibrillation threshold, maximal following frequency and effective refractory period (ERP-ms) were determined. Drug was infused, and electrical stimulation measurements were taken 3 min after increasing the dose of drug by doubling the rate of infusion (page 3). Surgically prepared animals were administered spiradoline and ECG measures were taken 5 min after beginning infusion. ECG, arrhythmia, BP, heart rate and mortality were monitored for 30 minutes after occlusion (page 4). ECG measures were influenced in a dose dependent manner by spiradoline. The highest dose produced a 59% increase in PR interval. The QRS width was prolonged by 57%. The QaT interval of the ECG, as well as the ERP, was prolonged by

spiradoline infusion. Rsh, an index of sodium channel blockade in the rat, also was increased in a dose-dependent manner by spiradoline (page 6). The pattern of action of spiradoline in isolated hearts and intact rats indicated that spiradoline may block both sodium and potassium currents. The effective refractory period, ERP, was also dose-dependently prolonged by spiradoline in the absence and presence of naloxone (page 7). Spiradoline reduced contractility and prolonged PR and QRS intervals of the ECG in isolated rat hearts, and in anesthetized rats increased RSh and QaT. Such changes were independent of k receptor actions because they occurred in the presence of naloxone. Thus, spiradoline induced sodium and potassium channel blockade in the heart, as seen with class I and III antiarrhythmic agents (page 11).

Accordingly, Pugsley discloses electrical-stimulation studies, including measurement of effective refractory period, and ECG measurements, such as PR interval, QaT interval, etc. in vivo in rats for the characterization of spiradoline, which was shown to induce sodium and potassium channel blockade in the heart.

Germann teaches that the mouse is the principal animal model for studying biologic processes in mammals, and that a variety of mouse strains harboring gene mutations leading to inherited developmental disorders have been designed, including ion channelopathies associated with human clinical phenotypes such as long QT syndrome, etc, creating mouse models of human electrophysiologic disease. Functional analyses of underlying molecular mechanisms of resultant phenotypes require appropriate and sophisticated experimental methodology. Genetic mouse models pertinent to human arrhythmogenic disorders and their application to present

day ex vivo and in vivo murine electrophysiologic technology at the whole organ and animal level are discussed (abstract). An in vivo epicardial and endocardial EP study is provided, in which mice are anesthetized with intraperitoneal pentobarbital and ketamine, and a multilead surface ECG is obtained by subcutaneous electrodes placed in each extremity. In the epicardial approach, epicardial pacing wires are placed directly on the surfaces of the right ventricular, left ventricular and right atrium. For intracardiac studies, a catheter is advanced from the right internal jugular vein through the right atrium to the right ventricle. The distal electrodes pace and record from the right ventricle, while the proximal electrodes pace and record from the right atrium. Catheter position is confirmed with characteristic ECG tracings. In murine studies, standard clinical pacing protocols are used to determine basic EP parameters. Unipolar and bipolar ECG and intracardiac recordings are obtained from the right atrium, left ventricle and left ventricle via the epicardial route and from the right atrium and ventricle via the endocardial route. Pacing thresholds are determined, and stimulation is performed at twice the diagnostic capture threshold. All ECG intervals (PR, QRS, QT, JT, etc) are calculated in standard fashion. Standard clinical EP parameters including sinus node function, AV nodal conduction properties and refractory periods are determined. To test for pharmacologic effects on basal ECG and EP parameters, medication can be administered intravenously, intracardiac via the end-hole catheter or by intraperitoneal injection. The EP protocol can then be repeated in the same fashion as in the baseline to determine changes in arrhythmia induction, conduction or refractoriness (pages 256-357). As mouse and human cardiac electrophysiology differ substantially, future trends

in genetic research may involve the use of larger transgenic animal models (rat, rabbit, pig, sheep) that will more closely approximate human physiology (page 365).

Pugley and German do not specifically recite characterization of a Kv1.5 antagonist compound by ECG and EP parameters, and Germann does not exemplify measurement of ECG and EP parameters in rat model, including electrode placement at the axillary and inguinal areas of the rat.

Knobloch teaches that inhibition of the cardiac Kv1.5 channel is considered a new promising atrial selective antiarrhythmic concept since this channel since this channel is presumed to contribute to atrial but not ventricular repolarization in the human heart. In a previous study in pigs, clear baseline differences in refractoriness between left and right atrium with shorter effective refractory periods (ERPs) of the left atrium associated with a high left atrial vulnerability for tachyarrhythmias. In a newly established model, I_{Kur} blockers S9947 and S20951 were determined. In pentobarbital anesthetized pigs, ERPs in free walls of both atria with S1-S2 stimulus method and QTc intervals were determined. I_{Kur} blockade showed prolonged atrial ERP. I_{Kur} blocker S20951 showed prolonged left vs. right ERP. In contrast to I_{Kr} blockade, I_{Kur} blockade inhibited left atrial vulnerability and had no effect on QT interval. Thus, blockade of I_{Kur} seems to be a promising atrial selective antiarrhythmic concept (abstract). See also materials and methods section. The I_{Kur} blockers S9947 and S20951 were atrial selective since they showed a marked prolongation of atrial refractoriness with no apparent effect on ventricular repolarization while atrial ERP-prolongation by I_{Kr} blockers was associated with expected increases in QTc interval in vivo in pigs (page 485-6).

Based on the atrial selective prolongation of EPR and demonstrated inhibition of left atrial vulnerability IKur channel blockers are a promising new type of atrial antiarrhythmic drug.

Rotolo teaches that in the art of electrographic recordings, one of the essential conditions for successful recording is the correct electrode positioning on the body (column 1, lines 5-10). Electrode placement according to international standards is set forth, including a series of electrodes V4, V5 and V6 level with the fifth intercostal space along the left hemiclave, front axillary and media lines and electrodes V7 and V8 on the inguinal part (column 40, lines 2+).

It would have been obvious to one of ordinary skill in the art at the time of the invention to determine in vivo cardiac electrophysiology profiles of a compound affecting a cardiac ion channel, such as potassium channel including Kv1.5, in rat upon administration of the compound and simultaneous measurement of atrial refractory period and electrocardiogram interval from the teachings of Pugsley, Gehrmann and Knobloch. One would have been motivated to do so because both Pugsley and Knobloch demonstrate the evaluation of parameters such as ERP and ECG parameters such as QT interval, PR interval, etc. are critical for determination of mechanism of action of candidate antiarrhythmic compounds. One would have had a reasonable expectation of success in doing so because Pugsley shows measurements performed in vivo in rat for characterization of a sodium and potassium channel blocker, and Gehrmann teaches that to test for pharmacologic effects on basal ECG and EP parameters, medication can be administered and the EP protocol can be repeated to

determine changes in arrhythmia inducibility, conduction or refractoriness. One of ordinary skill could have readily adapted the protocol of Gehrmann including catheter and electrode placement to rat because Pugsley shows similar measurements performed in vivo in rat, and also because Gehrmann teaches that mouse and human cardiac electrophysiology differ substantially, future trends in genetic research may involve the use of larger transgenic animal models (rat, rabbit, pig, sheep) that will more closely approximate human physiology. With regard to electrode placement, it would have been further obvious to include oppositely positioned axillary and inguinal areas because Rotolo shows that such areas are standard areas for electrode placement, and teaches that electrode placement is one of several essential conditions for successful electrocardiographic recordings.

Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Fermini *et al.* (US 6,214,810) in view of Pugsley *et al.* (*J. Cardiovascular Pharmacology*, 1998, 32(6), p. 863-874), in further view of Porter ("Rats and Mice," *Laboratory Animal Medicine and Science Series II*, 2000, p. 1-12).

Fermini teaches methods of treating or preventing atrial arrhythmias which utilizes compounds which are blockers of the ultra-rapidly-activating delayed rectifier K^+ current (I_{Kur}) of the human atrium in a use-dependent and/or rate dependent manner, and which provide the selective block preferentially at fast heart rates so that the effect is realized or maximized when required (abstract). Effects on heart rate, mean arterial pressure, electrocardiographic intervals and atrial, atrioventricular (AV) nodal and

ventricular electrophysiologic parameters can be assessed in chloralose-anesthetized dogs. Bipolar epicardial electrodes can be sutured onto the left atrium, right atrium and left ventricle for electrical pacing and for the introduction of extrastimuli for the measurement of atrial, ventricular and atrioventricular (AV) nodal excitation thresholds and refractory periods. The following indices of cardiac conduction and refractoriness can be determined before and after the cumulative intravenous administration of test agent at a pacing frequency of 2.5 Hz (CL 400 msec): atrial and ventricular excitation thresholds (AET and VET, respectively); atrial relative (ARRP, 2.times.AET) and effective (AERP, 10.times.AET) refractory periods; ventricular relative (VRRP, 2.times.VET) and effective (VERP, 10.times.VET) refractory periods; AH interval, an index of AV nodal conduction; HV interval, an index of His-ventricular conduction time; P-A interval, an index of intraatrial conduction; and H-EG interval, an index of ventricular conduction; and paced ECG QT interval. AV nodal functional refractory period (AVNFRP) and SA conduction time (SACT) can be determined by the introduction of atrial extrastimuli during sinus rhythm, and the monitoring of ventricular response. Electrocardiographic intervals can be determined during sinus rhythm; the rate-corrected ECG QTc interval was calculated as: $QTc = QT \text{ (msec)} / R\text{-}R \text{ (sec)}$. Test agent can be administered as cumulative i.v. doses of 1, 3 and 10 mg/kg, with each dose administered over a period of 15 min in a vehicle of PEG-200. Hemodynamic, electrocardiographic and cardiac electrophysiologic determinations can be made immediately following the infusion of each dose.

Fermini teaches testing of electrophysiology profiles of I_{Kur} blockade compounds in dogs, rather than in rat.

Pugsley discloses sodium channel-blocking properties of spiradoline, a kappa receptor agonist and its antiarrhythmic action in the rat (page 1). Male Sprague-Dawley rats were used for whole animal studies. Intact rats were anesthetized with pentobarbital and the trachea cannulated for artificial ventilation. The right jugular vein and left carotid artery were cannulated for administration of drugs and recording of blood pressure, respectively. ECG was recorded. By using intact rats described, electrical stimulation of the left ventricle was accomplished via two Teflon-coated silver wire stimulating electrodes inserted through the chest wall and implanted into the left ventricle. Ventricular fibrillation threshold, maximal following frequency and effective refractory period (ERP-ms) were determined. Drug was infused, and electrical stimulation measurements were taken 3 min after increasing the dose of drug by doubling the rate of infusion (page 3). Surgically prepared animals were administered spiradoline and ECG measures were taken 5 min after beginning infusion. ECG, arrhythmia, BP, heart rate and mortality were monitored for 30 minutes after occlusion (page 4). ECG measures were influenced in a dose dependent manner by spiradoline. The highest dose produced a 59% increase in PR interval. The QRS width was prolonged by 57%. The QaT interval of the ECG, as well as the ERP, was prolonged by spiradoline infusion. Rsh, an index of sodium channel blockade in the rat, also was increased in a dose-dependent manner by spiradoline (page 6). The pattern of action of spiradoline in isolated hearts and intact rats indicated that spiradoline may block both

sodium and potassium currents. The effective refractory period, ERP, was also dose-dependently prolonged by spiradoline in the absence and presence of naloxone (page 7). Spiradoline reduced contractility and prolonged PR and QRS intervals of the ECG in isolated rat hearts, and in anesthetized rats increased RSh and QaT. Such changes were independent of k receptor actions because they occurred in the presence of naloxone. Thus, spiradoline induced sodium and potassium channel blockade in the heart, as seen with class I and III antiarrhythmic agents (page 11).

Accordingly, Pugsley discloses electrical-stimulation studies, including measurement of effective refractory period, and ECG measurements, such as PR interval, QaT interval, etc. in vivo in rats for the characterization of spiradoline, which was shown to induce sodium and potassium channel blockade in the heart.

Porter teaches that rats and mice have several attributes that contribute to their popularity as research animals. They are well characterized and understood anatomically, physiologically, and genetically. They withstand inbreeding fairly well, and a large number of inbred strains have been established. Many mutant stocks that are models of human disease have also been established. Rats and mice are also hardy, adaptable, easy to care for and handle, and are inexpensive. Their small size means they can be housed in large numbers. Their short generation time and high reproductive potential contribute to their usefulness in genetics research and to the economy of their production. They are amenable to germfree and pathogen-free production techniques, thereby greatly reducing intercurrent disease as a variable (page 7).

It would have been obvious to one of ordinary skill in the art at the time of the invention to perform electrophysiology measurements, including electrophysiology interval and atrial period, for example, of I_{Kur} blockade compounds as disclosed by Fermini shown in dog model, in rat model when the teachings of Fermini are taken in view of Pugsley and Porter. One would have been motivated to do so because Porter teaches that rat animal models have advantages such as being hardy, adaptable, easy to care for and handle, inexpensive, and capable of being housed in large numbers. One would have had a reasonable expectation of success in doing so because Pugsley shows similar electrophysiology measurements upon administration of sodium and potassium channel blockers in rat.

Conclusion

No claims are allowed at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leah Schlientz whose telephone number is (571)272-9928. The examiner can normally be reached on Monday-Tuesday and Thursday-Friday 9 AM-5 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael G. Hartley/
Supervisory Patent Examiner, Art Unit 1618

LHS